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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,802	09/17/2001	Roland Kreutzer	33796	8835

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BOSTON, MA 02110

EXAMINER

VIVLEMORE, TRACY ANN

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/889,802	Applicant(s) KREUTZER ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 221-225, 232-239, 241-247, 249, 251-253 and 255-262 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 221-225, 232-239, 241-247, 249, 251-253 and 255-262 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

S.016

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Notice of Non-Responsive Amendment

Applicant's reply to the Notice of Non-responsive Amendment mailed February 7, 2005 is acknowledged. The text of claim 249 cited by the previous Examiner appears to have been properly amended. It is noted however, that the strike-through text of other claims present in the claim amendment of November 18, 2004 is replete with typographical errors and misspellings. Since the newly added text does not contain such errors, these claims have been examined on the merits, however Applicant is informed that any future claim amendments must be in full compliance with 37 CFR 1.121(c).

Specification

The objection to the specification set forth in the Office Action mailed June 14, 2004 is maintained for the reasons of record. See the related new matter rejection for response to Applicant's arguments.

Claim Objections

Claims 249 and 252 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Art Unit: 1635

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Each of these claims depend from claim 221 and recite the limitation that one strand of the dsRNA is fully complementary to less than the full-length of an RNA transcript of a mammalian target gene. These claims do not further limit claim 221, which already contains this limitation. It is further noted that the text of claims 249 and 252 is identical.

Claim Rejections - 35 USC § 112

The rejection of record of claims 221-225, 236-239, 241-245, 247 and 249-252 under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendment of November 18, 2004. However, new rejection under 35 USC 112, second paragraph are set forth below.

Claims 223, 236, 243, 245 and 247 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 223 and 243 each depend from claims 221 and 224. It is impossible to meet the limitations of both of these claims simultaneously because claim 221 consists of two strands and a 3' overhang while claim 224 consists of two strands, a 3' overhang and a linker. Similarly, claims 236, 245 and 247 each depend from both of claims 232 and 237. It is impossible to meet the limitations of both of these claims simultaneously because the cell of claim 232 contains an oligonucleotide that consists of two RNA strands and a 3' overhang

while the cell of claim 237 contains an oligonucleotide that consists of two RNA strands, a 3' overhang and a linker.

Response to Arguments- Specification & Claim Rejections - 35 USC § 112

Claims 221-225, 232-239, 241-245, 247, 249, and 251-253 are maintained as rejected and new claims 255-262 are rejected under 35 U.S.C. 112, first paragraph, as containing new matter for the reasons of record set forth in the previous Office Action.

1. Each of claims 221-225, 232-239, 241-245, 247, 249, 251-253 and 255-262 are directed to dsRNA oligonucleotides and cells comprising such oligonucleotides wherein the dsRNA has a 3'-overhang.

2. Applicant's arguments filed November 18, 2004 have been considered but they are not persuasive. Applicant argues that Example 1 of the specification provides inherent support for dsRNAs having a 3' overhang since the nature of the transcription protocol used and the promoters present in the vector would result in a U residue after the double stranded region and that digestion with RNase A, which cleaves only single stranded RNA, would produce a single nucleotide overhang due to cleavage after this U. This argument demonstrates that Applicants have support for a 3' overhang of a single U nucleotide. However, the claims as amended are not limited solely to single nucleotide overhangs, but recite 3' overhangs generically including overhangs of several nucleotides.

3. Applicant further argues that the disclosure provides support for the broad genus of compounds claimed, citing the existence of two examples, each of which provides a

Art Unit: 1635

double stranded RNA having a 3' overhang. This argument is not persuasive because the claims are directed to overhangs that are unlimited in length and can comprise any nucleotide or combination of nucleotides. Each of the examples disclosed in the specification results in a 3' overhang of a single U nucleotide. The disclosure in the specification does not provide support for overhangs of any nucleotide.

4. Applicant argues that the specification provides inherent support for a genus of dsRNAs having a 3' overhang. Applicant further states that because they have shown a reduction to practice they have shown possession of the claimed genus of compounds. These arguments are not persuasive because Applicant's disclosure is not commensurate in scope with the claims. Applicants have claimed a large genus of compounds that have a 3' overhang. This overhang is not limited by number or by composition of nucleotides present. The specification discloses examples of dsRNAs that have a single nucleotide overhang wherein the nucleotide is U. The specification provides no support for single nucleotide overhangs of other nucleotides nor does it provide support for overhangs of more than a single nucleotide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 224, 225, 237, 238, 243, 251 and 256 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550).

5. Claim 224 is directed to dsRNA consisting of two strands no more than 49 nucleotides in length having a 3' overhang wherein a linker connects the two complementary strands. Claim 225 limits claim 224 by reciting that the linker is polyethylene glycol. Claims 237 and 238 are directed to mammalian cells containing the dsRNA having a linker that may be polyethylene glycol. Claim 243 is directed to a composition of the dsRNA, claim 251 limits the length to 15-49 nucleotides. Claim 256 is directed to a dsRNA as in claim 224 wherein the overhang is a single nucleotide.

6. Agrawal et al. disclose self-stabilized oligonucleotides useful for antisense therapeutics that comprise a target hybridizing region and a self-complementary region. On page 9, line 30 through page 10 line 1 Agrawal et al. disclose that the target hybridizing region is complementary to a nucleic acid sequence from a variety of sources and is from 8-50 nucleotides in length. On page 15, line 26 through page 17, line 12 Agrawal et al. disclose that the self-complementary region of the oligonucleotide is fully or partially complementary to the hybridizing region, which encompasses oligonucleotides having 3' overhangs, the hybridizing region and the self-complementary region can be linked by a polyethylene glycol linker. Agrawal et al. administer such oligonucleotides to mammalian cells, thus disclosing the subject matter of claims 237 and 238.

7. Thus, Agrawal et al. disclose all limitations of and anticipate claims 224, 225, 237, 238, 243, 251 and 256.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

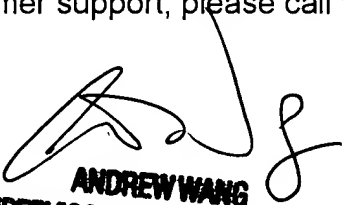
If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone

Art Unit: 1635

number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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Art Unit 1635

TV
May 20, 2005